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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/584,328      | 05/30/2000  | Kurt E. Petersen     | 22660-0026US        | 1737             |

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[REDACTED] EXAMINER

WARDEN, JILL ALICE

| ART UNIT | PAPER NUMBER |
|----------|--------------|
| 1743     | 5            |

DATE MAILED: 04/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 09/584,328             | PETERSEN ET AL      |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | Elizabeth Quan         | 1743                |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on \_\_\_\_\_.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-21 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 6/30/2000 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
 If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
 a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |   |  |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                               | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                      | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____                                     |

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## **DETAILED ACTION**

### *Oath/Declaration*

1. Applicant has not given a post office address anywhere in the application papers as required by 37 CFR 1.33(a), which was in effect at the time of filing of the oath or declaration. A statement over applicant's signature providing a complete post office address is required.

### *Drawings*

2. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they do not include the following reference sign(s) mentioned in the description: (2190B) first mentioned on line 5 of page 46. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

3. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference sign(s) not mentioned in the description: (162) and (164B) in FIG. 15A; (164A), (164B), and (166) in FIG. 15B; (56) in FIG. 21; and (53) and (56) in FIG. 22. A proposed drawing correction, corrected drawings, or amendment to the specification to add the reference sign(s) in the description, are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

4. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(4) because reference character "(50)" has been used to designate both inlet channel and outlet channel in lines 1-3 on page 30. Reference character "(188)" has been used to designate both valve actuator and spring in lines 1 and 2 on page 35. Reference character "(87)" has been used to designate both filter stack and chamber in line 3 on page 60. A proposed drawing correction or corrected

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drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

*Specification*

5. The disclosure is objected to because of the following informalities: In line 9 on page 68 "the" in between "detectors" and reference number (198) should be omitted.

Appropriate correction is required.

6. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

*Claim Rejections - 35 USC § 112*

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-11, 15, 17, 19, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 1 recites the limitation "the side walls" in the first line of sub-heading i) of the claim. There is insufficient antecedent basis for this limitation in the claim.

10. Claims 4 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: Are the "two additional side walls" part of the sidewalls in previously mentioned claims? Neither the specification nor drawings support additional

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sidewalls than those comprising the frame of the reaction vessel. The side walls in these claims have been interpreted as the side walls mentioned in previous claims for examination purposes.

11. Claims 8 and 19 recite the limitation "the sample" in the second line of sub-heading a). There is insufficient antecedent basis for this limitation in the claim.

12. Claims 6 and 17 recite the limitation "the first port" and "the second port" in the fourth and fifth lines of the claims. There is insufficient antecedent basis for this limitation in the claim. The claim could be made more clear and definite, as it is unclear whether the first and second ports are part of the "at least two separate ports" mentioned in the claim.

13. Claim 20 recites the limitation "the inner surface of the plates" in the second line of the sub-heading c). There is insufficient antecedent basis for this limitation in the claim.

14. Claims 2, 3, 5, 7, 9-11 are rejected based upon rejection of base claim 1.

***Claim Rejections - 35 USC § 102***

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1-4, 6-15, and 17-21 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,674,743 to Ulmer.

Referring to claims 1-4, 6-15, and 17-21, Ulmer discloses an apparatus for automated DNA sequencing, which comprises a cleaving station (50), transport system (70), and detection station (90) (see ABSTRACT; FIG. 7; COL. 16, lines 14-16).

Cells are introduced into sample chamber (52) consisting of a small depression in a substrate at the edge of a transparent cover plate (see FIG. 7; COL. 19, lines 14-16). Cells may be monitored by the microscope system equipped with an infrared single-beam gradient optical trap (see COL. 19, lines 25-27). The microchannels may have electrodes for providing an electric field to the sample fluid, which causes the cells to migrate single-file into the exit capillary channel (53) (see COL. 19, lines 56-61). The target cell for sequencing is identified by visual inspection using the microscope (65), and the target cell is confined in the optical trap and translated along the exit channel (53) to the cell isolation chamber (56) (see COL. 19, lines 63 and 64; COL. 20, lines 2-4). A bifurcation (54) in the capillary channel allows for sorting or selection of specific cells for sequencing via diverting a cell into one branch or the other of the capillary channel by applying an electric field along the selected branch (see COL. 20, lines 7-14). With the isolation of a target cell in chamber (56), an appropriate culture medium to replicate DNA to the point of metaphase is introduced into the chamber through another microchannel (57) (see COL. 20, lines 25-32). Subsequently, cells may be lysed through chemical and/or physical techniques (see COL. 20, lines 45-51). When the cell has been disrupted and the chromosomes are released, the chromosomes are separated into individual compartments (see COL. 21, lines 9-11). Individual chromosomes are captured and transported in microchannel (58) to isolation chamber (60) via a single-beam gradient optical trap (see COL. 21, lines 9-16). The DNA is confined in an extended conformation in a narrower capillary channel (62) with the end of the DNA distal from the exonuclease binding site is immobilized on a microscopic bead (68) and

the other end with a single bound molecule of exonuclease (67) positioned at the mouth of microchannel (72) at the nozzle (80) (see COL. 22, lines 56-61; COL. 30, lines 27-33). Nucleotides (64) are cleaved from DNA strand (66) at the nozzle (80) in microchannel (72), and the nucleotides are detected by detection station (90) (see COL. 30, lines 34-36).

A flow cell (500), which has a nozzle (72) and heating element (73) adapted to mate with the opening of microchannel (75), extends from the micromachined body of the cleaving station (50), incorporates elements of the transport system (70), and provides access to the nucleotide-containing matrix (88) for the detection and identification at the detection station (90) (see FIGS. 7-12 and 15; COL. 16, lines 36-39; COL. 32, lines 54-58; COL. 33, lines 27-29). Flow cell (500) comprises three sheets (510,520,530) made of glass, which has a certain degree of rigidity or flexibility (see FIG. 15; COL. 33, lines 6 and 7). Sheets (510,530) form major walls sandwiching sheet (520) with connecting sidewalls angularly offset from each other by about 90 degrees (see FIG. 15). Microchannel (76) is disposed in the lower two sheets (520,530), wherein the upper half of the channel is in sheet (520) and the lower half of the channel is in sheet (530) (see FIG. 15; COL. 33, lines 23-25). Sheath fluid (77) enters microchannel (76) at port (78) at constant laminar flow rate (see COL. 31, lines 39 and 40). Microchannel (75) is formed in sheet (530) (see FIGS. 7 and 15; COL. 33, lines 62-64). A nucleotide stream enters the center of a coaxial sheath solution in the same direction in microchannel (75) through nozzle (80) (see COL. 17, lines 1-3).

Radiation from a radiation source (92) is directed to matrix (88) in microchannel (76) in the bottom of sheet (530) by external lens, which also collects the fluorescent emission from individual nucleotides (64) in matrix (88) for detection by detection system (94) (see FIGS. 7-12 and 15; COL. 33, lines 34-38; COL. 37, lines 49-64; COL. 39, lines 42-55). Optical access to matrix (88) may also be provided on the upper surface of the flow cell (500) by imaging through the glass refrigerator (510) and upper sheet of the flow channel (520) or through sheets (520,530) by one or more waveguides (95) defined in the sheets (see FIGS. 7-12 and 15; COL. 33, lines 39-44). The entire flow cell (500) is contained within a stainless steel vacuum dewar to thermally isolate the flow cell (500) from the ambient environment (see COL. 33, lines 45-49). The dewar has optical windows positioned over the flow cell (500) to provide optical access for fluorescence detection of nucleotides (64) and manipulation of the DNA molecule (66) by an optical trap (69) operating on the optical handle (69) (see COL. 33, lines 49-54).

The upper sheet (510) contains a refrigeration system (85), which comprises a gas inlet (511), gas outlet (512), countercurrent heat exchanger (514), expansion capillary (516), and reservoir (518) (see FIG. 15; COL. 33, lines 7-11). For a cooling effect a high pressure gas is supplied to inlet (511) which goes through the countercurrent heat exchanger (514) to the expansion capillary (516), where it expands and cools (see FIG. 15, COL. 33, lines 13-16). The gas enters reservoir (518) and the cooled vapor reenters the heat exchanger (514) to outlet (512), precooling incoming gas (see FIG. 15; COL. 33, lines 16-18). The refrigeration system is operated in an open cycle with the pressurized gas supplied by a high pressure tank and provides a steep temperature gradient between

the nozzle (80) and point of fluorescence excitation in the detection (90) (see COL. 32, lines 38-42; COL. 33, lines 20-22).

***Claim Rejections - 35 USC § 103***

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

18. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 5 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,674,743 to Ulmer.

Referring to claims 5 and 16, Ulmer discloses a dewar containing a flow cell (500) provided with optical access for purposes of fluorescence detection of nucleotides (64) and manipulation of the DNA molecule (66) by an optical trap (69) operating on the optical handle (68) (see COL. 33, lines 49-54). To maximize the light collection efficiency of the objective lens, a high numerical aperture is desired (see COL. 33, lines 54 and 55). Minimizing the working distance between the objective lens and the matrix (88) is also desired and may be accomplished by using a minimal thickness window in the vacuum dewar, minimizing the vacuum gap between the inside surface of the window and the surface of the flow cell (500), and minimizing the thickness of the sheet (530) along with the depth of its microchannel (76) (see COL. 33, lines 49-64). Ulmer does not quantify the width and thickness of the flow cell (500). Applying the decision of *In re Aller*, discovering the optimum workable range of the width and thickness of the chamber involves only routine skill in the art. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to determine through experimentation a width to thickness ratio of 4:1 and a thickness range of 0.5 to 2 mm to maximize the light collection efficiency of the objective lens and minimize the working distance between the objective lens and matrix to achieve greater sensitivity.

***Double Patenting***

21. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

22. Claims 1-21 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 136-168 of copending Application No. 09/194374. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims address the same elements with the same limitations, such as a reaction vessel with a rigid frame and optically transmissive side walls or a heating element to induce a temperature change within the chamber of the vessel.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### *Conclusion*

23. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The prior art contains one or more limitations recited in the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Quan whose telephone number is (703) 305-1947. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (703) 308-4037. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7718 for regular communications and (703) 872-9311 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1193.

Elizabeth Quan  
Examiner  
Art Unit 1743

eq  
April 2, 2002

  
Jill Warden  
Supervisory Patent Examiner  
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